

Applying Legacy Statutes to Modern Modalities: Adapting US PTE Law for Complex Biologics

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Presenter



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Agenda

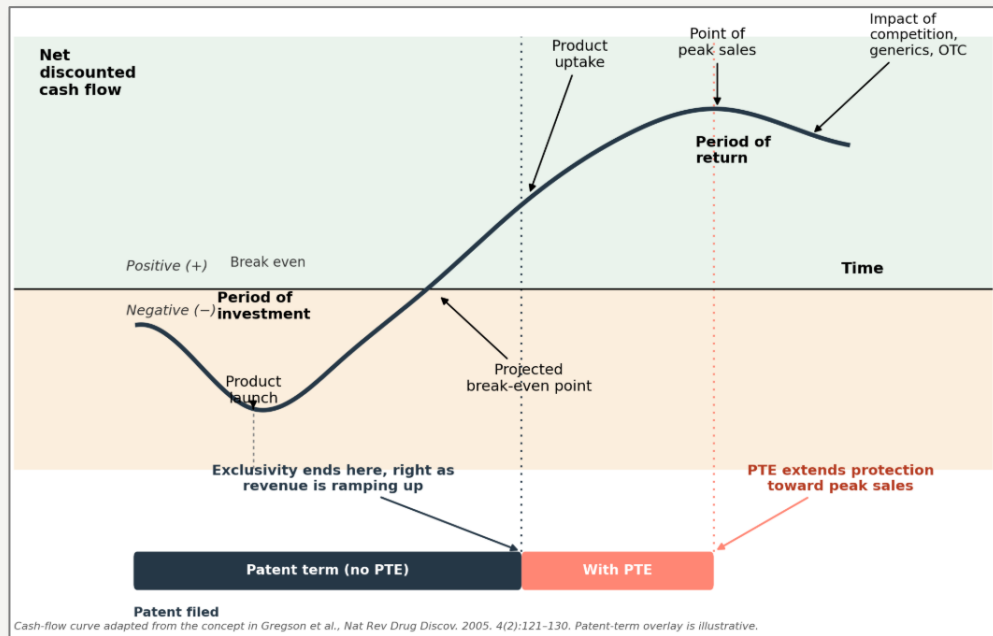
- US PTE Basics
- PTE Eligibility - Active Ingredient
- Eligible Patents for PTE
- Claim Scope During PTE
- Portfolio Strategy



Why PTE Matters

THE STAKES

- Revenue for drugs and biologics is not uniform over the patent term
- Pre-launch: \$0, launch is contingent on clinical testing and FDA review during the patent term
- **Example: Humira®**
 - 2018–2022: approximately \$58 million per day
 - Last 5 years of exclusivity: approximately \$100 billion
- The patentee is effectively deprived of its ability to exploit its invention during the statutory patent term because it is legally prohibited from marketing the product
- PTE compensates by restoring a portion of the post-issuance time consumed by regulatory review



Patent Term in the United States

- **Patent Term Adjustment (“PTA”)**

Compensates for examination delays caused by the USPTO

- **Patent Term Extension (“PTE”)**

Compensates for delays at other agencies, particularly FDA





US PTE Basics

Eligibility

- Patent term extension available for patents related to new:
 - Human drugs, antibiotics, and biological products
 - Animal drugs
 - Veterinary biological products
 - Food/color additives
 - Medical devices subjected to premarket approval (“PMA”) procedures



US PTE Basics

Eligibility (cont'd)

A patent is eligible for PTE only if:

- The patent claims a product, method of using a product, or method of manufacturing a product;
- The product has been subject to a regulatory review period;
- The regulatory review results in the first permitted commercial marketing/use of the product (or, for method of making patents, of a product made by the manufacturing method);
- The patent is unexpired before PTE application filing; and
 - Can request “interim” PTE between 6 months and 15 days of patent expiration
- The patent has never been granted PTE before



US PTE Basics

Calculation of Term

PTE term is equal to the portion of the regulatory review period (“RRP”) after the patent’s issue date except:

- Only one patent can be extended for the same RRP;
 - But note that separate drug products (e.g., formulations) of the same active ingredient can be subject to separate RRP
 - May submit multiple patents for consideration and elect one at the end of the process if more than one is eligible for PTE
 - Must inform the USPTO if doing so
- Period of extension cannot exceed **five years**;
- Total patent term post-approval may not exceed **14 years**;
- PTE reduced by periods when applicant did not act with due diligence; and
- Patent receives PTE for only half the time spent in trials before filing an application for FDA approval (*e.g.*, an NDA or BLA)



US PTE Basics

Calculation of Term (cont'd)

- $PTE = 0.5 * TP + AP - DD$
- Extension = Factor of “Testing period” and “Approval period”
 - Testing period (TP): IND effective date → NDA/BLA submission.
 - Approval period (AP): NDA/BLA submission → NDA/BLA approval.
 - Due Diligence (DD): Period Applicant did not act with due diligence.
 - Counting only days after the patent is issued.
 - Reissue does not change original issue date. *Merck Sharp & Dohme B.V. v. Aurobindo Pharma USA, Inc.*, 23-2254 (Fed. Cir. 2025).



PTE Eligibility - Active Ingredient

Applied to Complex Biologics



PTE Eligibility

Product Eligibility

- First permitted commercial marketing/use of the “product”
- What is a “product”
 - A drug product
 - Any medical device, food additive, or color additive
- What is a drug product?
 - The term “drug product” means the active ingredient of—
 - a new drug, antibiotic drug, human biological product,
 - including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient

Product → Drug Product → Active Ingredient

???



PTE Eligibility

Eligibility for Small Molecule Drug(s)

- Product: the active ingredient or salt/ester
 - Active ingredient needs to be present in the approved product (cannot be a metabolite)
- Has the product (active ingredient) not been previously approved for commercial marketing?
 - Small Molecule Drugs - **including any salt or ester of the active ingredient**
 - Active ingredient is **not active moiety** (*Photocure ASA v. Kappos* (2010))

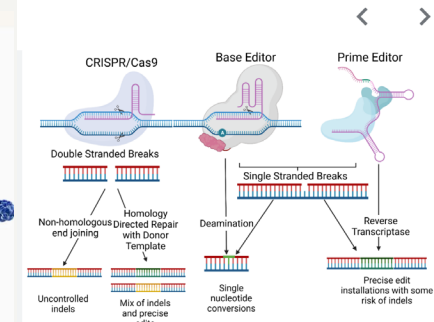
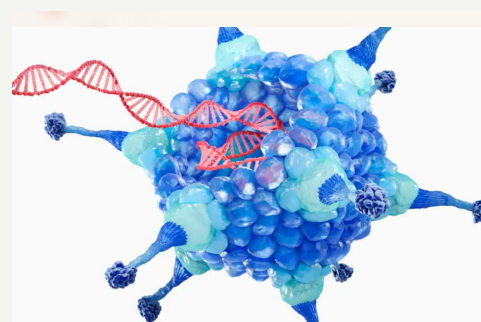
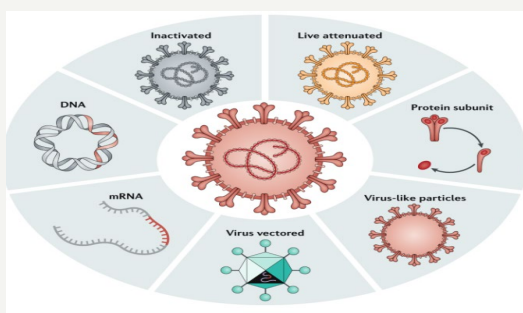
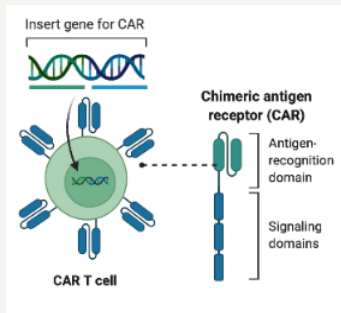
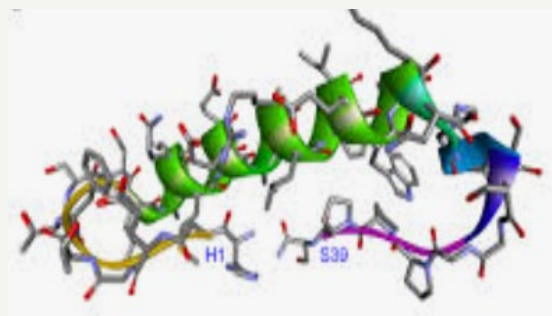
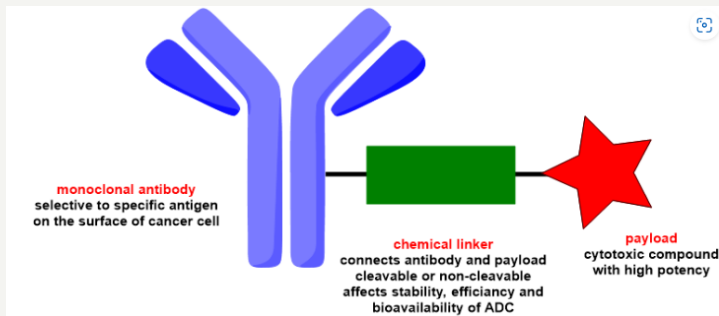
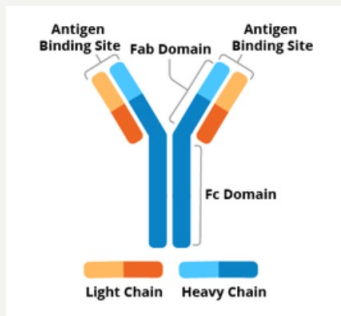
Your Product	Previously approved	First approval of the product?
Salt	Free base	✓
Ester	Free base	✓
Free base	Salt	x
Free base	Ester	x
Salt B	Salt A	✓
Ester	Salt	✓
Salt	Ester	✓
Salt	Ester-salt	x
Co-Crystal of crystal A and crystal B	Crystal A and Crystal B	TBD (SEGLENTIS: co-crystal of celecoxib and tramadol hydrochloride)



PTE Eligibility

Biologics Eligibility – active ingredients

- What is an Active Ingredient for a Biological Product:





PTE Eligibility

Biologics Eligibility – active ingredients

- Protein/antibody-based therapies
 - Heterogenous population in primary sequences, post translational modification (e.g., glycosylation), etc.
 - Batch variation in clinical drug product
- Biologics with multiple levels of components that can be considered as an “active ingredient”
 - Cell therapy
 - The Cell?
 - The CAR expressed by the cell?
 - The nucleic acid encoding the CAR?
 - Gene therapy
 - The viral particle?
 - The gene product?
 - The nucleic acid encoding the gene product?



PTE Eligibility

Biologics Eligibility – first approved commercial use

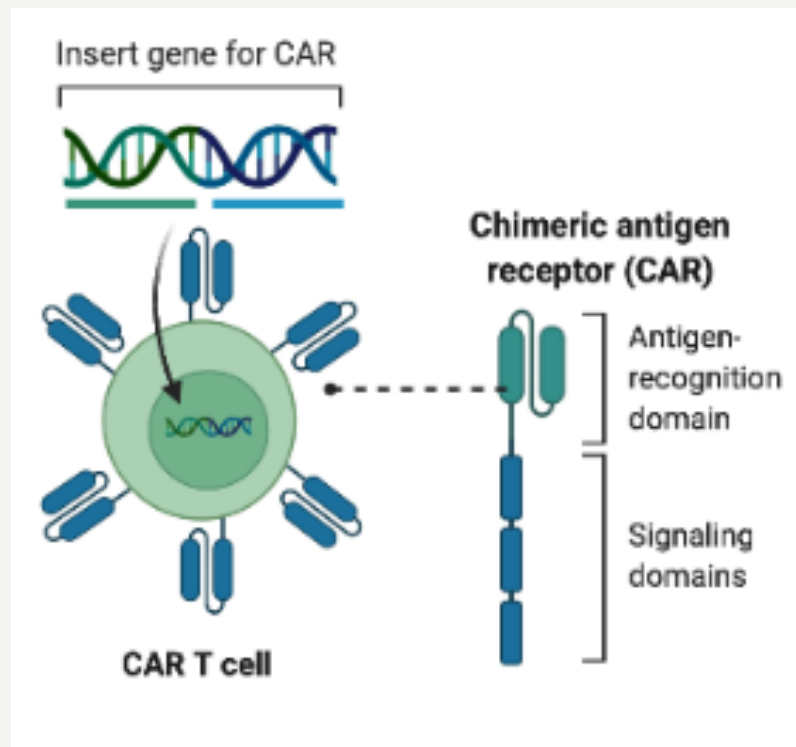
- Has the Biological product (**active ingredient**) not been previously approved for commercial marketing
 - Antibody Examples
 - Avastin (bevacizumab) and Lucentis (ranibizumab)
 - A previously approved antibody v. its serum half-life extended version?
 - mRNA vaccine Examples
 - Different mRNA vaccines encoding the same antigen
 - Cell therapy Examples:
 - Previously approved antigen binding domain of the CAR
 - Previously approved CAR-T having the same antigen binding domain



PTE Eligibility

Biologics Eligibility – Case Study

- YESCARTA®: *Autologous* CAR-T Cell; US7741465B1
- Challenges
 - What is the Active ingredients and has it been previously approved
 - Not the CAR-T cell due to patient-to-patient variation
 - Not the CAR due to lack of description to distinguish from previously approved product
 - Four FDA-approved CAR T cell therapies (Kymriah, Yescarta, Tecartus, Breyanzi) based on the same anti-CD19 scFv
 - DNA sequence encoding the CAR – **Bingo but potentially with limited scope of protection**
 - Sufficient details of the active ingredient in the PTE application
 - Inconsistency in USPTO/FDA's determination of an active ingredient
 - LAVIV® (Axficel-T): autologous fibroblasts listed as active ingredient was acceptable to USPTO in PTE application





Eligible Patents for PTE

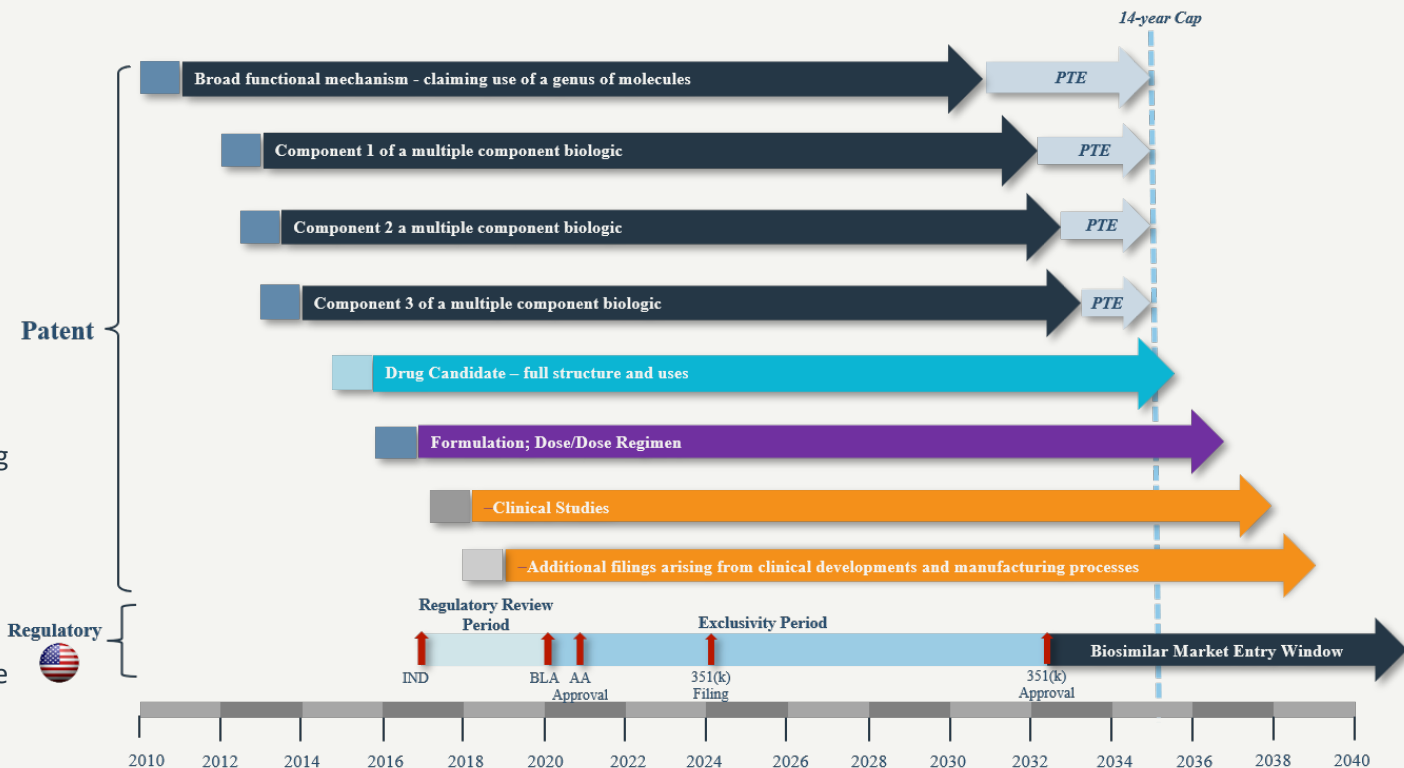
Applied to Complex Biologics



Eligible Patents for PTE

The patent “claims” a product, method of using a product, or method of manufacturing a product

- “Claims” **historically** mean “encompasses”
 - *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997) holds patent claiming a metabolite of a drug product isn’t eligible for PTE
- Small molecule: usually the patent that claims the specific compound structure or a method of use
- **Biologics?**

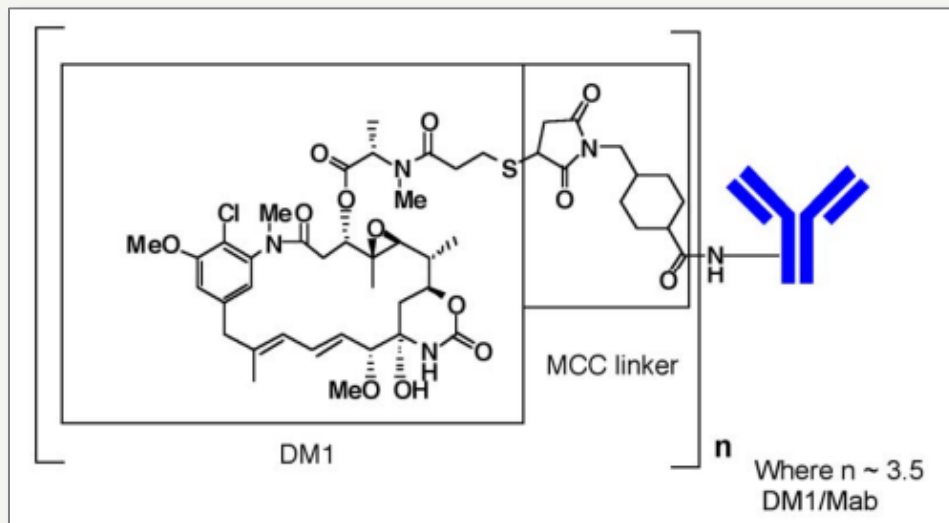




Example PTE claims

Kadcyla (ado-trastuzumab emtansine) approved in 2013

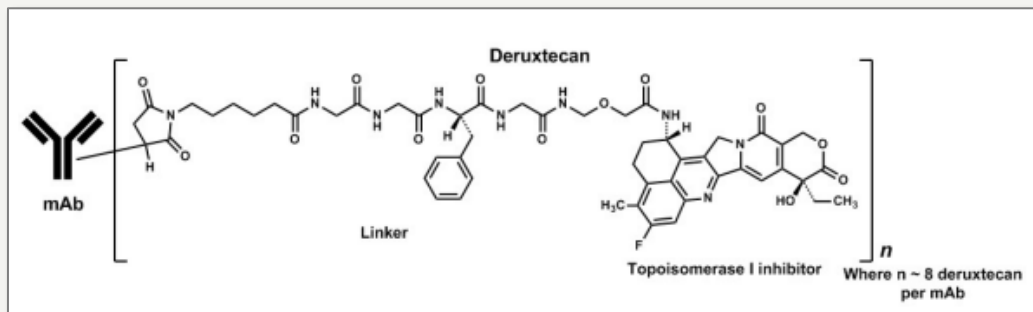
- US7097840B2 (expires 7/25/2026 with 682 days of PTA and 1275 days of PTE)
 - A method for the treatment of a tumor in a mammal, comprising the steps of (i) identifying said tumor as being characterized by overexpression of an ErbB2 receptor and as being a tumor that does not respond, or responds poorly, to treatment with an anti-ErbB2 antibody which binds to the 4D5 epitope and which has a growth inhibitory effect on SK-BR-3 cells, and (ii) administering to a mammal having said tumor a therapeutically effective amount of a conjugate of an anti-ErbB2 antibody which binds to the 4D5 epitope with a maytansinoid.
- PTE patent application states claims 1, 3, 6-17, 20-26, 28, 29, and 42-44 claim the use of API
 - Claim 17 identifies the antibody by clone name
 - Claim 22 identifies the payload
 - Claim 24 identifies the linker





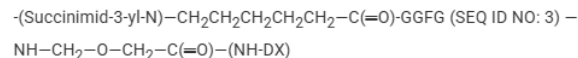
Example PTE claims

ENHERTU (fam-trastuzumab deruxtecan-nxki) approved in 2019



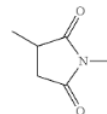
- US10155821B2 (expires 12/20/2033 with 0 days of PTA and 71 days of PTE)
 - 20-year term expires 1/28/2035
 - TD filed against 9872924 and 9808537 (exp. 10/10/2033)
- PTE application states all claims claim the API

1. An antibody-drug conjugate, wherein a linker and an antitumor compound represented by the following formula and anti-HER2 antibody are connected:

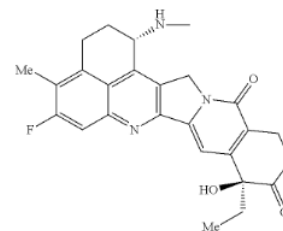


wherein

-(Succinimid-3-yl-N)- has a structure represented by the following formula:



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1, and (NH-DX) represents a group represented by the following formula:

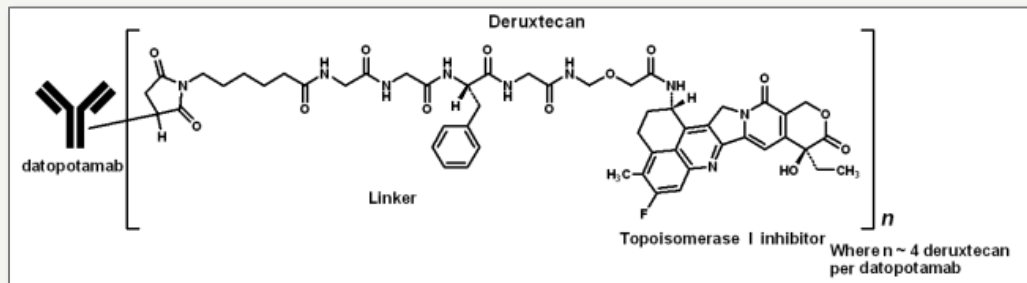


wherein the nitrogen atom of the amino group at position 1 is the connecting position.



Recent USPTO Trend

Datroway (datopotamab deruxtecan-dlnk) approved 2025



PTE application submitted in US10195288B2

- Identifies claims 1, 2, 4-9, 13-16, 25, and 31-33 as reading on the product, and claim 17 as reading on a method of using it
- None of the claim specifically provide the antibody sequences

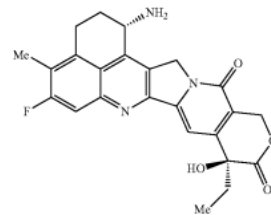
On 6/16/2026, the USPTO issued a final determination stating that the '288 patent is not eligible for PTE because it does not "particularly point[s] out and distinctly claim[s] the drug"

- Citing *Teva v. Amneal Pharmaceuticals*, 124 F.4th 898 (Fed. Cir. 2024) relating to orange book listing
- Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997) sets forth "claims the product" isn't the same as "is infringed by the product"

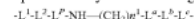
Uncharted territory - how specific does it need to be???

The invention claimed is:
1. An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 1]



is conjugated to an antibody via a linker having a structure represented by the following formula:



wherein the antibody is connected to the terminal of L^1 , the antitumor compound is connected to the terminal of L^6 with the nitrogen atom of the amino group at position 1 of the antitumor compound as the connecting position,

wherein

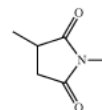
L^1 represents $-(Succinimid-3-yl-N)-(CH_2)n^2-C(=O)-$ wherein n^2 represents an integer of 2 to 8,

L^2 represents $-NH-(CH_2-CH_2-O)n^3-CH_2-CH_2-C(=O)$ or a single bond, wherein n^3 represents an integer of 1 to 6,

L^3 represents a tetrapeptide residue of GGFG, $-NH-(CH_2)n^4-L^5-L^6-$ is $-NH-(CH_2)_3-C(=O)-$, $-NH-CH_2-O-CH_2-C(=O)-$, or $-NH-(CH_2)_2-O-CH_2-C(=O)-$,

$-(Succinimid-3-yl-N)-$ has a structure represented by the following formula:

[Formula 2]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.



Claim Scope During PTE

Does it cover a biosimilar?



Claim Scope During PTE

Does it cover Biosimilar?

- Claim scope during PTE is limited to the “product” (active ingredient) and its approved use
- Case law in the small molecules space makes it clear active ingredient is any component that is intended to furnish pharmacological activity or other direct effect and it must be present in the drug product when administered. The active ingredient is defined by what is approved and is specified on the drug’s label.
 - *Biogen v. Banner*, 956 F.3d 1351 (Fed. Cir. 2020)
- “Biosimilar” definition contains no requirement of being structural identical
 - (A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and
 - (B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product."



Portfolio Strategy

Complex Biologics



Portfolio Strategy for Complex Biologics

Maximize Patent Exclusivity

- Unlike small molecule drugs, PTE may not be the most reliable way to maximize patent exclusivity of a complex biologic drug
- Strategies for complex biologics
 - Also keep patent exclusivity in mind when developing/maturing a patent portfolio
 - Prepare multiple patents with varying claim scope that are eligible for PTE
 - Maximize PTE period of these patents by aligning prosecution with regulatory timelines
 - Manage obviousness double patenting issues
 - Continue to build in layers of patent protection with 154 term extends beyond what PTE can provide
 - Where applicable file biosimilar directed patent applications

